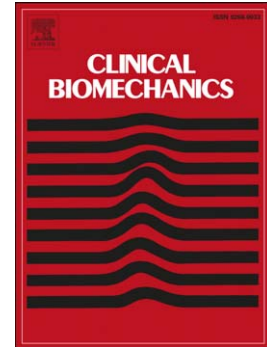


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Varus thrust in women with early medial knee osteoarthritis and its relation with the external knee adduction moment

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Abstract

Background: Varus thrust, defined as an abrupt increase of the knee varus angle during weight-bearing in gait, has been shown to be present in patients with moderate to severe knee osteoarthritis and is considered to be one of the risk factors for progression of symptomatic medial knee osteoarthritis. We evaluated the presence and magnitude of varus thrust and its relation with the Knee Adduction Moment in women with early medial knee osteoarthritis, and compared it to that in a group of controls and in a group of subjects with established medial knee osteoarthritis.

Methods: Twenty-seven women with early medial knee osteoarthritis, 20 women with established medial knee osteoarthritis and 24 asymptomatic controls were evaluated. Varus thrust was estimated as an increase of the knee varus angle during the weight-bearing phase of gait at self-selected speed, assessed by 3D motion analysis.

Findings: Varus thrust was significantly higher in both early and established osteoarthritis groups compared to the control group ($p < 0.001$), but not different between osteoarthritis groups. While the knee adduction moments were higher than controls only in the established osteoarthritis group, the magnitude of varus thrust was significantly correlated with the second peak knee adduction moment.

Interpretation: Higher varus thrust was found both in early and established stages of knee osteoarthritis, suggesting that problems with dynamic stabilization of the knee are present early in the development of knee osteoarthritis. This highlights the necessity of considering dynamic alignment in rehabilitation already in the early stages of the disease.

Keywords: Gait analysis, stability, alignment, Knee adduction moment

1. Introduction

Knee osteoarthritis (OA) is one of the major causes of disability in the elderly population, affecting a greater proportion of women than men [1, 2], whereby the medial knee compartment is among the most affected sites [3]. Knee joint alignment has been put forward as one of the risk factors for knee OA [4, 5] and several authors have reported an association of increased static knee varus alignment with increased OA severity [6, 7]. Malalignment of the knee either in varus or valgus direction influences the load distribution over medial and lateral compartments of the knee joint [8]. A neutrally aligned knee bears approximately 60-80% of the compressive load on the medial compartment [9] and a 5 degrees increase in varus alignment results in a 20% increase of load on the medial compartment [8]. Such an increase in medial compartment loading will put extra stress on articular cartilage and the subchondreal bone and might subsequently lead to degenerative changes.

Assessment of knee alignment using standing radiographs comes with some limitations such as availability and exposure to radiation [10]. Moreover, the alignment is affected during the radiography by foot position [9] and weight-bearing status [10]. Furthermore, since pain and functional limitations during dynamic activities are the major complaints among subjects with knee OA, assessment of the change in alignment during functional activities such as gait could provide essential information.

Varus thrust is a dynamic malalignment of the knee that has been defined as an abrupt increase of the knee varus angle when the leg is bearing weight, with a decrease during the non-weight-bearing phase of ambulation (swing phase) [11, 12]. In a prospective study, the presence of varus thrust was shown to be related to disease progression [11]. Also, an association between pain and varus thrust in subjects with knee OA has been reported previously [13]. Varus thrust can be quantified as the difference between the knee adduction angle at heel contact and the maximum knee adduction angle during the early stance phase of gait [11, 12]. Only a few previous studies investigated varus thrust in OA [11-14] and in some of these only the presence

of varus thrust was studied by visual observation and not by quantitative motion analysis [11, 13, 14]. However, neither the presence nor the magnitude of varus thrust have been investigated in the early OA population [15].

Varus thrust has been associated with a higher external knee adduction moment (KAM), a proposed non-invasive indirect index of the load on the medial compartment of the knee joint [11, 12]. Barrios et al. found that the peak knee adduction angle during gait was more strongly related to the KAM than static radiographic alignment [16]. There are reports on the absence of higher KAM early in the disease process, which might imply that the KAM may not be increased in the early stages of knee OA [17], which would suggest that it is a consequence rather than a cause of OA progression. Therefore, it is important to assess varus thrust and KAM in patients with early knee OA. Quantification of varus thrust in the early stages of the disease, will provide further insight into the profile of early OA. Future longitudinal studies can then further investigate the potential role of dynamic alignment in the transition of early OA to established OA.

In the present study, we investigated static knee alignment and varus thrust in subjects with early medial knee OA, classified based on the presence of pain and a combination of early structural changes detected on radiography and Magnetic Resonance Imaging (MRI) [15], and this was compared to subjects with established knee OA and asymptomatic controls. Furthermore, we studied the relationship between static alignment and varus thrust on one hand and KAM on the other hand. We defined varus thrust as the increase in varus angle between heel contact and its peak value during stance and also investigated the presence of varus thrust by dichotomizing the varus thrust as either present (above the median of all subjects) or not present (below the median of all subjects).

We hypothesized that, 1) varus thrust would be more common and the magnitude of varus thrust would be higher in subjects with medial knee OA compared to the asymptomatic controls, 2) the differences expected based on hypotheses 1 would also exist between established and

early OA patients, 3) there would be a positive correlation between the magnitude of varus thrust and KAM.

2. Materials and Methods

Forty-seven women with medial knee OA (27 with early and 20 with established OA) 24 healthy controls participated in this study. All participants were informed about the study procedure and signed informed consent forms. The study was approved by the ethical committee for Biomedical Sciences of the KU Leuven in Belgium prior to testing and was conducted in agreement with the principles of the Declaration of Helsinki.

Participants with knee OA were recruited during their visit to a rheumatologist or orthopedic surgeon in the University Hospitals Leuven, and they were further sub-classified, into early ($n = 27$) and established ($n = 20$) medial knee OA groups, based on the classification system introduced by Luyten et al. [15]. The inclusion criteria for the early OA group were: presence of knee pain, a Kellgren & Lawrence (K&L) grade 0, 1 or 2- (osteophytes only) for the medial compartment on radiography and presence of two of four MRI criteria: (1) \geq Boston-Leeds Osteoarthritis Knee Score (BLOKS) grade 2 for size cartilage loss, (2) \geq BLOKS grade 2 for percentage full-thickness cartilage loss, (3) signs of meniscal degeneration and (4) \geq BLOKS grade 2 for size of bone marrow lesions (BMLs) in any one compartment. Participants in the healthy control group ($n = 24$) were recruited through social organizations. The inclusion criteria for the control group were as follows, K&L grade 0 or 1 on the radiography of either knee, asymptomatic, no history of knee OA or other pathology involving any lower extremity joints.

Each participant was referred for a physical exam and bilateral standard anterior-posterior weight-bearing radiographs in fixed flexed position were obtained (Siemens, Siregraph CF, Agfa CR HD5.0 detector 24*30). Diagnosis and categorization of knee OA were based on the K&L

grading system [18] and a single experienced observer (FPL) graded each radiograph. A magnetic resonance image (MRI) was taken from the (most) affected side of the OA patients, based on radiography, and a random side in the control group. A 3.0 Tesla scanner (Philips Achieva TX, Philips Medical Systems, Best, The Netherlands) with an eight-channel phased array knee coil was used, and subjects were scanned in a non-weight bearing supine position, as described by Baert et al. [19].

The standardized BLOKS scoring system was used by two separate readers (NN, GVDS) to score structural features of the tibiofemoral joint [20]. On 91% of all scored items, the two readers had full agreement and disagreements were resolved by consensus.

The classification of participants in the established knee OA group was based on the slightly adjusted American College of Rheumatology (ACR) classification criteria [21], which includes knee pain, age above 50, stiffness less than 30 minutes and crepitus, combined with structural changes defined as presence of minimum grade 2+ (osteophytes and joint space narrowing), on K&L scale for the medial compartment on radiography, indicating a moderate to severe disease severity. Patients with higher K&L grade on the lateral than on the medial compartment of the same knee were excluded.

2.1. Assessment of knee symptoms and function

All participants completed the Dutch version of Knee Injury and Osteoarthritis Outcome Score (KOOS). This version has been shown to be valid and reliable for patients with knee OA [22]. The KOOS has five distinct sections. To evaluate the knee OA signs and symptoms, the subscales 'pain' and 'symptoms' were used. The 'ADL' section was used to estimate participants' subjective physical performance. A converted score from 0 to 100 was computed for each subscale, with 100 indicating the best possible result.

2.2. Assessment of static knee joint alignment

The static alignment of the knee joint was assessed by an experienced musculoskeletal radiologist on full-leg AP weight-bearing plain radiographs of the lower extremities [23]. Malalignments of less than -2° or more than $+2^{\circ}$ were categorized as valgus or varus alignment respectively. Knee alignment between -2° and $+2^{\circ}$ was classified as neutral [4, 24].

2.3. Gait data acquisition and analysis

A 3D motion analysis system (Krypton, Metris and Vicon Nexus, Oxford Metrics Group) was used to record the spatial position of markers on relevant body segments at 100 samples/s. Ground reaction forces were recorded through force plates (Bertec Corporation, Ohio, USA and AMTI, Watertown, MA, USA) placed in a 12m walkway at a sample rate of 1000 samples/s. Participants walked along the walkway at a comfortable habitual speed during gait analysis. To avoid force plates being targeted while performing the trials, no guidance on walking, except the instruction to 'walk naturally' was provided. Three complete force plate strikes for each foot were registered. Since footwear can affect the distribution of loads on the joints in the lower quadrant [25], all participants were asked to walk bare-footed. The "heel-strike" event was detected as the first sample of vertical ground reaction force that was above 10 N. The "toe-off" event was chosen as the first sample at which the vertical ground reaction force was below 10N [26]. 3D Cardan angles of the knee were calculated using the decomposition order according to Grood & Suntay [27]. External knee adduction moment (KAM) was calculated through a bottom-up dynamic linked segment model, using kinematics of the body segments and the ground reaction forces [28]. To obtain the knee adduction moment from the 3D components of the net moments, the knee moments were projected onto the calf coordinate system. Extracted external knee adduction moment was normalized to body mass.

2.4. Assessment of dynamic knee joint alignment

Varus thrust magnitude was calculated as the difference between the knee adduction angle at heel strike and the first maximum knee adduction angle during the stance phase of gait (Figure 1) [11, 12]. Varus thrust was subsequently dichotomized into groups of subjects with and without varus thrust, based on the median value of varus thrust (2.02°) in the whole group of subjects [29].

2.5. Statistical analysis

Statistical analyses were performed using SPSS software (version 20, 2006, Chicago: SPSS Inc) and for all tests, p values less than 0.05 were considered statistically significant. Means and standard deviations were calculated and one-way analyses of variance (ANOVA) were used to test for group differences in height, weight, age, BMI. A Kruskal-Wallis test was used to test for differences between the three groups for KOOS sub-scores. Gait related, as well as static alignment, group differences were tested using Generalized Estimating Equations (GEE) with *Group* as factor and age, height, and weight as co-variables. Furthermore, the magnitude, as well as the presence of varus thrust was compared between those with and without static varus alignment. Static alignment was also included as covariate when testing group differences for varus thrust. Relations between static alignment, varus thrust, and presence of varus thrust on one hand, and the first and second peak in the KAM on the other hand were assessed using univariate and multivariate linear regression analyses over the patients' group (early and established OA).

3. Results

As presented in Table 1, the three groups were comparable in age, height, weight, and BMI. Both OA groups had significantly more knee pain ($P < 0.001$, for both) and more symptoms ($P_{\text{established}} < 0.001$ and $P_{\text{early}} = 0.002$) compared to asymptomatic controls, but without significant differences between the two OA groups (table 1). OA patients also demonstrated worse self-reported physical performance ($P < 0.001$, for both) and Quality of Life (QoL) ($P < 0.001$, for both), than controls. Preferred walking speed and stance time were not significantly different between the three groups ($P = 0.32$ and $P = 0.44$, respectively).

3.1. Static knee joint alignment

Static alignment was significantly different between the three groups, with the established OA group showing significantly higher varus malalignment compared to the early OA group and the healthy controls ($p = 0.002$ and $p < 0.001$, respectively). There was no significant difference between the early OA and control groups ($p = 0.202$). In the control group, 79% and in the early OA group, 74% of the subjects had a neutral alignment; in the established OA group, 48% of the subjects showed varus malalignment and 48% showed a neutral alignment (Table 1).

3.2. Dynamic knee joint alignment

Knee adduction angles increased after initial stance phase in all three groups (figure 1.A). The amount of varus thrust was 1.41° (0.3), 2.58° (0.4), 3.26° (0.5), for the control, early OA, and the established OA groups, respectively (figure 2).

Subjects with early and established knee OA showed significantly higher values of varus thrust compared to the asymptomatic control group ($p = 0.019$ and $p = 0.001$, respectively) (Figures 2.A & 3). There was no significant difference in varus thrust magnitude ($p = 0.197$) between the two

OA groups. After adjustment for age, height, weight, and static alignment, the differences between the early and the established OA groups on one hand and the control group on the other hand were still significant ($p = 0.028$ and $p = 0.009$, respectively). The amount of varus thrust was significantly higher in subjects with static varus malalignment (mean (SD) = 3.8° (0.5°)) compared to the subjects with neutral static alignment (mean (SD) = 2° (0.3°)) ($p = 0.005$) also after adjustments for age, height, and weight ($p = 0.037$).

The presence of varus thrust was significantly more common in the early OA group and the established OA group, compared to the controls ($p = 0.033$ and $p = 0.008$, respectively). No such difference for the presence of varus thrust was found between the two OA groups ($p = 0.454$).

The presence of varus thrust was significantly higher in subjects with static varus malalignment (median (IQR) = 0 (1)) compared to the subjects with neutral static alignment (median (IQR) = 1 (0)) ($p = 0.003$). Results stayed the same after adjustments for age, height, and weight ($p = 0.002$).

3.3. External knee adduction moment

There were no differences between groups in the magnitude of the first peak of the KAM. The second peak of the KAM was different between groups; subjects with established knee OA demonstrated a significantly higher second peak compared to subjects with early medial knee OA and to the healthy controls ($p = 0.011$ and $p = 0.004$, respectively) (Figure 4). There was no such difference between the early OA group and the asymptomatic controls ($P = 0.684$) (Figure 4).

3.4. Correlations between knee alignment and external knee adduction moment

There was a significant correlation between the static alignment and the first peak KAM over the patients group ($p = 0.018$, $r = 0.345$). The static alignment showed also significant correlations with the second peak KAM ($p = 0.021$, $r = 0.336$).

There was a trend towards a significant correlation between the magnitude of varus thrust and the first peak KAM over the patients group ($p = 0.057$, $r = 0.28$). The magnitude of varus thrust also showed significant correlations with the second peak KAM ($p = 0.037$, $r = 0.306$).

Analysis of dichotomized varus thrust showed that the groups with a larger than median varus thrust had significantly higher first and second peaks of the KAM ($p = 0.01$ and $p = 0.033$, respectively).

Table 1. Subject's clinical characteristics

		Control (n = 24)	Early OA (n = 27)	Established OA (n = 21)	P-value	P Established vs. control	P Early vs. control	P Early vs. established
Weight (kg) ^a		65.71 (9.6)	72.52 (11.9)	69.94 (10.9)	0.089			
BMI (kg/m ²) ^a		24.81 (0.8)	27.45 (0.7)	27.16 (0.8)	0.073			
Height (m) ^a		1.63 (0.06)	1.63 (0.05)	1.6 (0.07)	0.291			
Age (years) ^a		63.95 (1.8)	67.38 (1.1)	66.05 (1.6)	0.068			
K&L score (MC) ^c		Grade 0: n=18 Grade 1: n= 6	Grade 0: n= 10 Grade 1: n= 18 Grade 2: n= 1	Grade 2+: n= 15 Grade 3: n= 6				
KOOS Pain ^b		100 (4.9)	80.5 (33.4)	81.9 (28.5)	<0.001	<0.001	<0.001	0.471
KOOS Symptoms ^b		92.8 (10.8)	82.1 (25)	83.9 (29.4)	<0.001	<0.001	0.002	0.216
KOOS ADL ^b		100 (2.6)	89.7 (29.4)	86.7 (33.1)	<0.001	<0.001	<0.001	0.64
KOOS QoL ^b		100 (4.7)	75 (43.8)	59.4 (60.9)	<0.001	<0.001	<0.001	0.407
Static alignment ^c	Neutral Valgus Varus	n= 19 n= 4 n= 1	n= 20 n= 3 n= 4	n= 10 n= 1 n= 10				
Self-selected walking speed (m/s) ^a		1.24 (0.2)	1.21(0.2)	1.15 (0.2)	0.32			
Stance time (sec) ^a		63.81 (5.8)	64.82 (5.7)	66.04 (6.4)	0.44			

OA=osteoarthritis; BMI= Body Mass Index; K&L= Kellgren & Lawrence (range 0-4), KOOS = Knee injury and Osteoarthritis Outcome Score.

Data are presented as ^aMean (SD), ^bMedian (IQR) or ^cfrequencies. The P value corresponds to ^aANOVA test or ^bKruskal-Wallis test (with post hoc tests) comparing the three groups.

[†] Significant difference between groups (P < 0.05).

4. Discussion

To the best of our knowledge, this is the first study that assessed the magnitude of varus thrust in a sub-population of subjects with early medial knee OA. Results showed that varus thrust is more common and that the magnitude of varus thrust is greater in women with early medial knee OA than in healthy controls, as it is in women with established medial knee OA. While a relation between peak KAM and varus thrust was found, peak KAM were higher compared to control in established OA only.

The magnitude of varus thrust reported in the current study corresponds to previously reported values [12]. Consistent with our finding, previous results also reported that varus thrust is more common and has a larger magnitude in subjects with established medial knee OA than in healthy controls [11-13]. Increased varus thrust observed in the two OA groups in the current study might partly be due to greater static varus alignment in this group. However, the difference was still significant when corrected for static alignment. Increased varus thrust, suggests a decreased control over knee joint motion in the frontal plane in subjects with knee OA, which has been associated with decreased proprioceptive acuity and reduced muscular strength [14, 30]. Further studies are needed to determine the causes of the increased varus thrust in OA patients.

In line with the present results, previous studies have already shown that the magnitude of varus thrust is significantly correlated with the external KAM [11, 12]. This might imply that varus thrust, by shifting the ground reaction force towards the medial compartment, may expose the knee joint to higher medial joint loading [11, 12, 31]. This is further highlighted by the greater adduction moment in knees with varus thrust compared to knees without varus thrust. It should be noted that the present results show the increased varus thrust is already present in the early stage of OA, while increased KAM is only present in the more established phase,

suggesting that increased varus thrust precedes changes in the KAM or that varus thrust is more sensitive to knee OA than KAM.

The presence of significantly elevated first and second peak KAM in subjects with varus thrust, based on dichotomized varus thrust data, suggest that visual observation of thrust during gait could offer a simple clinical tool to detect subjects at higher risk of developing excessive medial joint load. This would not require quantitative gait analysis or radiographic assessment of knee mechanical alignment. However, the validity and reliability of visual observation would need to be verified.

Current results suggests that the effort to stabilize the knee in the frontal plane both in early and established OA groups is not adequate to prevent the varus thrust and consequently counteracting greater KAM. Therefore, development and validation of specific exercise regime that targets frontal plane dynamic instability, especially at the early stages of the disease process, seems necessary in order to slow down the knee OA progression by reducing the chance of developing greater medial loads. Patients with higher/presence of varus thrust can also benefit from stabilizing orthoses or probably lateral wedged insole, as it has been shown to be effective in reducing the greater force associated with varus thrust [32].

There are some limitations to our study and hence the conclusions that may be drawn from our data. First, although the classification criteria for early OA have been proposed as a result of several rounds of discussion (Delphi approach) between rheumatologists and orthopedic surgeons, it is still in its early days and further prospective validation of this classification is needed. Second, in the current study barefoot walking has been chosen, as footwear can affect the distribution of loads on the joints in the lower quadrant, however this limits generalization of the results. Therefore, our results may not apply to all real-life walking conditions, where shoes are worn. Also, the same relationships cannot be assumed to occur in shod conditions, as KAM may be influenced by several other covariates that have been shown to differ between shod and barefoot walking e.g., cadence, stride length and vertical ground reaction forces. Third, in

the current study, we did not correct the P-value, as this is an exploratory study and we were concerned of a possibility of occurrence of Type II errors due to very low corrected P-values. But, we avoided any P-hacking and reported all significant as well as non-significant results, so that the readers can make their own judgment based on the whole picture and not just some selected results. Moreover, since very few data were available on the expected results in this patient population, the statistical planning was limited and more a best guess exercise. We decided to work with sample size that were in line with published literature, as this is was an exploratory trial, and we tried to keep the patient population rather homogeneous. Also the fact that we found significant differences between early or the established OA groups compared to the controls, regarding varus thrust magnitude, as well as significant differences between the established OA and the early OA group, regarding 2nd peak KAM, suggests that the statistical power was adequate to see the differences between the two OA groups. Finally, as only women were included in this study, generalization of the current results to men should be treated with care.

5. Conclusions

We evaluated the presence and magnitude of the varus thrust in women with early medial knee OA and compared it to a group of asymptomatic controls as well as to a group of subjects with established medial knee OA. Results showed that the varus thrust is more common and that magnitude of varus thrust is significantly larger in subjects with early knee OA, as well as in established OA, even after adjustment for static alignment, compared to healthy controls. This study, along with the previous reports of varus thrust, further highlights the value of measuring thrust as a clinical index for medial knee OA.

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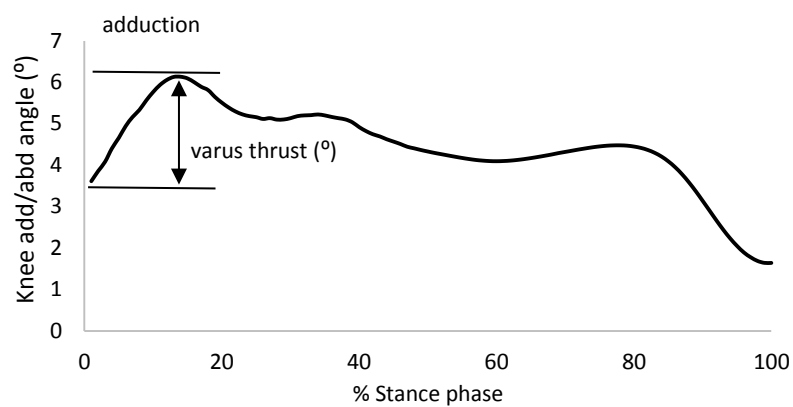


Figure 1. Varus thrust magnitude calculated as the difference between the knee adduction angle at heel strike and the first maximum knee adduction angle during the stance phase of gait.

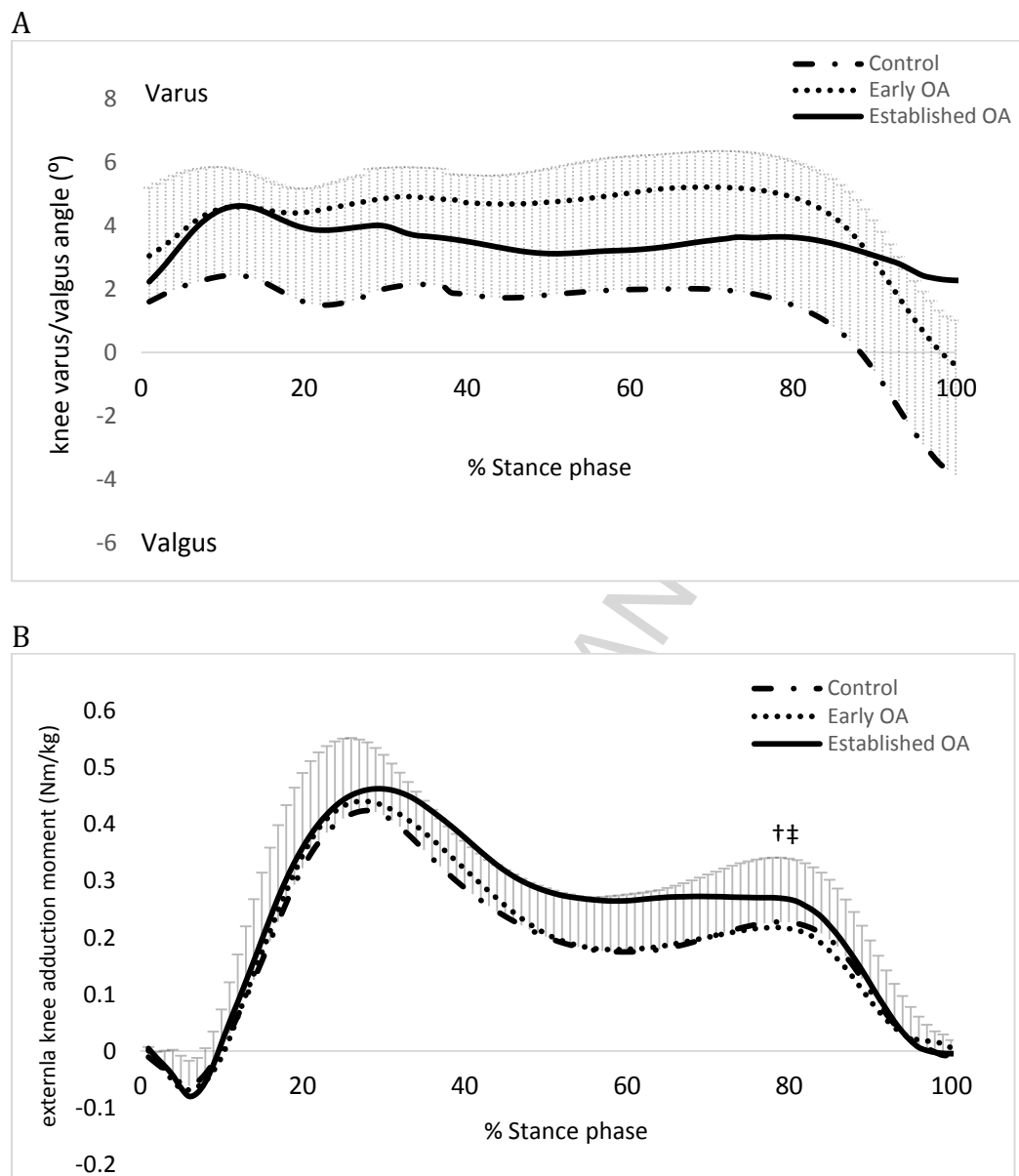


Figure 2. Mean waveform of the knee abduction-adduction angle for the early OA (...), established OA (_), and control group (_ .) with standard deviation of the control group (thin vertical lines) are compared for knee abduction-adduction angle (varus is in the positive direction) (A), external knee adduction moment (B).

† significant difference between established OA group and control group based on GEE with post hoc test ($P < 0.05$)

‡ significant difference between early OA group and control group based on GEE with post hoc test ($P < 0.05$)

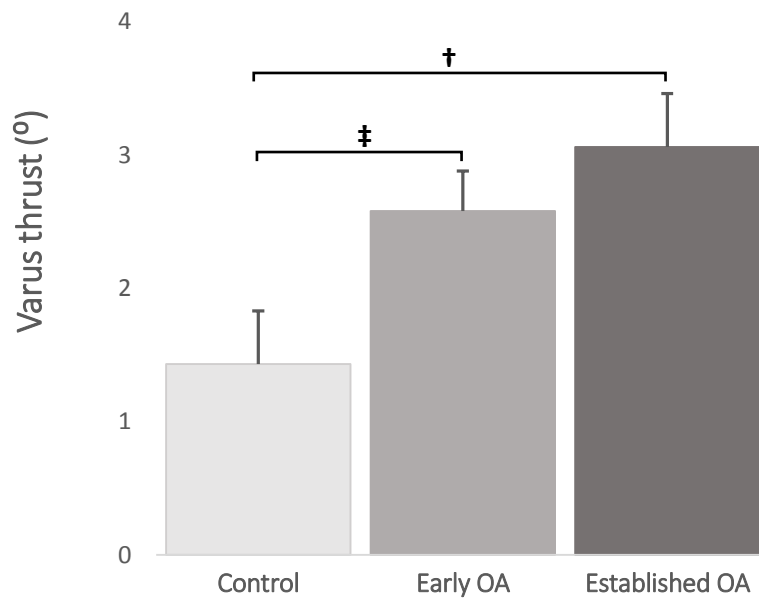


Figure 3. Mean and standard deviation for the varus thrust during stance phase of gait, of the early OA group, established OA group, and control group were compared.

† significant difference between established OA group and control group based on GEE with post hoc test ($P < 0.05$)

‡ significant difference between early OA group and control group based on GEE with post hoc test ($P < 0.05$)

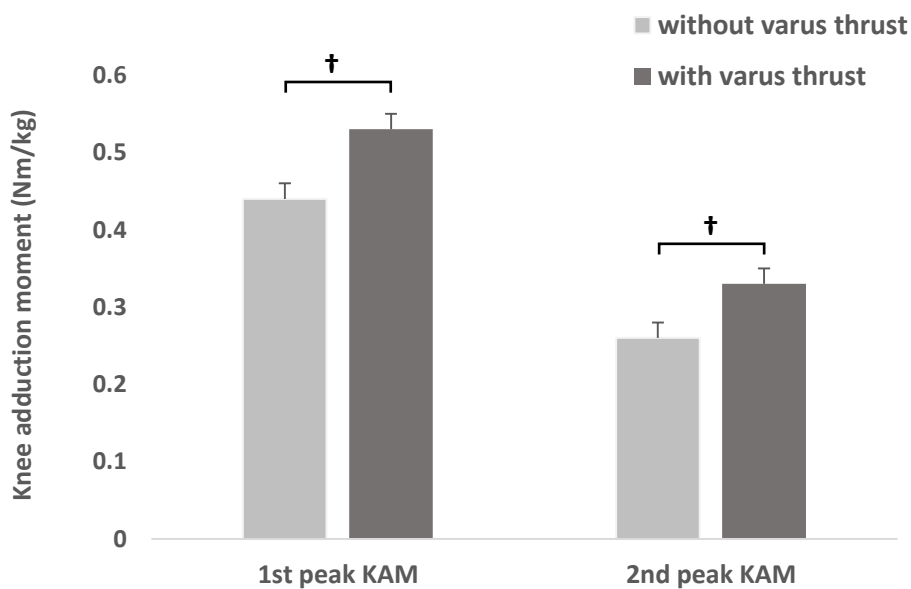


Figure 4. Mean and standard deviation for the first and second external knee adduction moment during stance phase of gait, of the two groups with and without varus thrust were compared.

† significant difference between subjects with and without varus thrust based on GEE ($P < 0.05$)

Highlights

- The presence & magnitude of varus thrust in early knee osteoarthritis investigated.
- The relation between varus thrust and knee adduction moment was also studied.
- Higher varus thrust was found both in early and established knee osteoarthritis.